(19) World Intellectual Property Organization International Bureau





(43) International Publication Date 12 September 2002 (12.09.2002)

(10) International Publication Number WO 02/069903 A3

(51) International Patent Classification7: A01N 43/04, A61K 31/70, C07H 1/00, 15/00, 17/00, 19/00, 21/00, 23/00, C07G 11/00, 3/00

(21) International Application Number: PCT/US02/06551

(22) International Filing Date: 6 March 2002 (06.03.2002)

English (25) Filing Language:

(26) Publication Language: English

(30) Priority Data: 6 March 2001 (06.03.2001) US 60/273,342 24 April 2001 (24.04.2001) US 60/285,698 211 60/331,323 14 November 2001 (14.11.2001)

(71) Applicant (for all designated States except US): BIOCRYST PHARMACEUTICALS, INC. [US/US]; 2190 Parkway Lake Drive, Birmingham, AL 35244 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): MONTGOMERY,

John, A. [US/US]; 2215 Brookshire Place, Birmingham, AL 35213 (US). BABU, Yarlagadda, S. [IN/US]; 3441 Strollway Drive, Birmingham, AL 35226 (US). ROWLAND, R., Scott [US/US]; 3436 Tamassee Lane, Hoover, AL 35226 (US). CHAND, Pooran [US/US]; 509 Creekwood Place, Birmingham, AL 35226 (US).

(74) Agent: AMERNICK, Burton, A.; Connolly Bove Lodge & Hutz LLP, P.O. Box 19088, Washington, DC 20036 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO. NZ. PL. PT. RO. RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent

[Continued on next page]

(54) Title: NUCLEOSIDES, PREPARATION THEREOF AND USE AS INHIBITORS OF RNA VIRAL POLYMERASES

$$R = H, \frac{O}{|I|} OR^3$$
 (II)

(57) Abstract: The compounds represented by the formulae (I) wherein X is selected from the group consisting of: O, S, N-R1, and CHR1; Y and Y' is individually selected from H, OR1, NR1R2, and N3 Z and Z' is individually selected from H, OR1, and NR1R2 R = H, formula (II), formula (III), or formula (III), R1 and R2 is selected from H, alkyl, acyl, aryl which may be substituted or unsubstituted, R3 is selected from H, alkyl, alkenyl, alkynyl, aryl, acyloxyalkyl, and pivaloyloxyalkyl, B is selected from 5 or 6-substituted uracil or cytosine, pseudouracil, N-substituted pseudouracil, 2-thiouracil, 2-thiocytosine, 5- or 6-substituted 2-thiouracil and 2-thiocytosine, 6-azauracil, 5-azacytosine, 8-azapurines, and 7-aza-8-deazapurines. Substitutions may be halosubstituted alkyl, halosubstituted alkenyl, halosubstituted alkynyl, halosubstituted aryl, alkylthio, or NR1R2. When Z and Z' are H and Y or Y' is OH then B is not 5-methyl uracil or cytosine; and pharmaceutically acceptable salts thereof, mono, di or triphosphate and prodrugs thereof.

WO 02/069903 A3



(BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, (88) Date of publication of the international search report: NE, SN, TD, TG).

27 February 2003

Published:

with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

BEST AVAILABLE COPY

INTERNATIONAL SEARCH REPORT

International application No.

	,	PCT/US02/0655	1
A. CLASSIFICATION OF SUBJECT MATTER IPC(7) : A01N 43/04; A61K 31/70; C07H 1/00, 15/00, 17/00, 19/00, 21/00, 23/00; C07G 11/00, 3/00; US CL : 514/42, 43, 45, 48, 49, 50, 51; 536/1.11, 4.1, 17.1, 22.1 According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED			
	=		
Minimum documentation searched (classification system followed by classification symbols) U.S.: 514/42, 43, 45, 48, 49, 50, 51; 536/1.11, 4.1, 17.1, 22.1			
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched			
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) WEST, REGISTRY			
C. DOCUMENTS CONSIDERED TO BE RELEVANT			
Category *	Citation of document, with indication, where ap		Relevant to claim No.
X,P	US 6,348,587 B1 (SCHINAZI et al) 19 February 200	2 (19.02-2002), columns 10-12 and	1, 4-8, 14-16
Ÿ	US 6,348,587 B1 (SCHINAZI et al) 19 February 2002 (19.02-2002), columns 10-12 and 1, 4-8, 14-16 22-23		
x	US 6,063,628 A (LOEB et al) 16 May 2000 (16.05.2000), column 3, lines 37-67; column 1, 4-6, 15-17, 19-20		
Ÿ	10, lines 13-53.		7-9, 11, 22-23
x	US 5,726,174 A (KIM et al) 10 March 1998 (10.03.1998), column 3, lines 35-67; column		1, 4-6, 14-16, 18, 20
Y	8, lines 19-32; column 9.		7-8, 10, 12, 22-23
· Parking to			
Further documents are listed in the continuation of Box C. See patent family annex.			
* Special categories of cited documents: "T" "A" document defining the general state of the art which is not considered to be of narticular relevance		"T" later document published after the in date and not in conflict with the app principle or theory underlying the in	lication but cited to understand the
		"X" document of particular relevance; it considered novel or cannot be consi when the document is taken alone	
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)		"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination	
"O" documen	t referring to an oral disclosure, use, exhibition or other means	being obvious to a person skilled in	
"P" document published prior to the international filing date but later than the priority date claimed		"&" document member of the same patent family	
Date of the actual completion of the international search 14 June 2002 (14.06.2002)		Date of mailing of the international search report 05 SEP 2002	
	ailing address of the ISA/US	Authorized officer	
Commissioner of Patents and Trademarks		$\sim 11/1$	Cellers &
Box PCT Washington, D.C. 20231		Patrick T. Lewis	Lellon b
		Telephone No/ 703-308-0196	
Form PCT/ISA/210 (second sheet) (July 1998)			

THIS PAGE BLANK (USPTO)